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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/448,649	05/24/95	MASINOVSKY	B 27866/32663

EXAMINER: GAMBEL, P

18M1/1003

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ART UNIT	PAPER NUMBER
1806	29

DATE MAILED: 10/03/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 9/19/97 (8/22/97 AMENDMENTS AND DECLARATIONS)

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 30-33 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 30-33 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-421-632/40201

DETAILED ACTION

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 9/19/97 (Paper No. 28) has been entered.

2. Applicant's amendment, filed 9/19/97 (Paper No. 28), is acknowledged.
Claims 30, 32-33 have been amended

Claims 30-33 are pending and being acted upon presently.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 9/19/97 (Paper No. 28), The rejections of record can be found in the previous Office Actions (Paper Nos. 21,24,27).

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 4.

5. Claims 30-33 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "a method of blocking interaction between bone marrow stromal cells expressing VCAM-1 and a cell expressing VLA-4 (wherein the cell expressing VLA-4 is a hemopoietic precursor cell) (wherein the cell expressing VLA-4 is a hemopoietic precursor cell expressing CD34 antigen) which comprises administering an antibody to VCAM-1 in an amount effective to decrease VCAM-1-mediated adhesion between the bone marrow stromal cell and the cell expressing VLA-4".

Applicant 's amendment, filed 9/19/97 (Paper No. 28) similarly to applicant's amendment, filed 12/12/96 (Paper No. 23), has directed support for the amended claims to the following.

(1) page 4, lines 11-16; however said passage refers to blocking lymphocyte binding to activated bone marrow stromal cells and not hemopoietic precursors;

Applicant also argues that the expression of VLA-4 on lymphocytes is noted throughout the specification. However, the claims are drawn to "cells", "a hemopoietic precursor cell", or "a hemopoietic precursor cell expressing CD34 antigen". The examiner agrees that the instant specification discloses inhibiting lymphocyte adherence and migration, however the claims are not drawn to lymphocytes but rather drawn to cells other than lymphocytes. For example, as previously noted; page 14, lines 28-32 similarly refers to blocking lymphocyte adhesion and not hemopoietic precursors.

(2) page 5, lines 14-15 which refers to Figure 12 as described in Example 5 and page 17, lines 24-30 which states: "VLA-4 ... is expressed at high levels on bone marrow cells bearing the CD34" and "that CD34 expression distinguishes a subset of bone marrow cells (1-4% which are enriched in primitive stem cells and progenitors"

In contrast to applicant's reliance on the instant disclosure including Example 5 and the expression of VLA-4 on hemopoietic cells; the specification provides guidance and direction to applying the use of VCAM-1-specific antibodies to prevent GVHD (page 18, lines 11-12) as well as to prevent modulating the immune response or to impede lymphocyte or tumor cell transmigration (see Summary of the Invention, particularly page 4, lines 17-22). With respect to the use of hemopoietic cells, the specification provides guidance and direction to immunoselecting primitive hemopoietic stem cells, progenitor cells and bone marrow stromal elements (page 18, lines 13-15).

Therefore, the examiner maintains that there does not appear to be support for interfering with hemopoietic cell-stromal cell interactions with VCAM-1-specific antibodies nor is there support how the skilled artisan would use such procedures. The inhibition of adhesion mediated by VCAM-1-specific antibodies as disclosed in the specification as filed is directed towards inhibiting lymphocyte adhesion such as useful in inhibiting GVHD and not towards inhibiting hemopoietic stem and/or progenitor cell adhesion.

Applicant is required to cancel the new matter in the response to this Office action.

6. Applicant 's amendment, filed 9/19/97 (Paper No. 28), also relies upon the submission or applicant's arguments and declaratory evidence, filed 8/22/97 (Paper No. 26).

Applicant's amendment in conjunction with the Torok-Storb and the Papayannoupoulo declarations under 37 C.F.R. § 1.132, filed 8/22/96 (Paper No. 26), have been fully considered but are not found convincing.

Similar to her previous declaration (Paper No. 20), Torok-Storb states that one of ordinary skill in the art would understand from reading the application that anti-VCAM antibodies are useful for blocking any VCAM-1-mediated adhesion, regardless of the type of cells involved and that one of ordinary skill in the art would have extrapolated results associated with blocking one VLA-4-VCAM-1 interaction to another (Paper No. 26).

Papayannoupoulo states that in light of the knowledged conveyed by the application, one of ordinary skill in the art as of the priority date would readily have been able to administer an amount of anti-VCAM-1 antibody effective to achieve the therapeutic endpoint, which is the decrease of VCAM-1-mediated adhesion between stroma and hemopoietic precursors, resulting in mobilization of hemopoietic cells. This declaration also relies upon evidence that the systemic administration of anti-VCAM-1 antibodies can release bone marrow progenitor cells from the marrow to the peripheral blood.

The examiner maintains that the application as filed does not provide written description nor guidance and direction on "how to use" anti-VCAM-1 to block any VCAM-1-mediated adhesion, regardless of the type of cells involved, to release bone marrow progenitor cells from the marrow to the peripheral blood or to mobilize hemopoietic cells.

As pointed out above in section 5 and of record, the specification provides guidance and direction to applying the use of VCAM-1-specific antibodies to prevent GVHD (page 18, lines 11-12) as well as to prevent modulating the immune response or to impede lymphocyte or tumor cell transmigration (see Summary of the Invention, particularly page 4, lines 17-22). With respect to the use of hemopoietic cells, the specification provides guidance and direction to immunoselecting primitive hemopoietic stem cells, progenitor cells and bone marrow stromal elements (page 18, lines 13-15).

Again, an amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. This is not the same from introducing subject matter never present in the specification as filed where no apparent error existed. Obviousness is not the standard for addition new limitations to the disclosure as filed. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Adding information to the specification not supported by the disclosure as filed is considered new matter in that introduces new concepts violate the description requirement of the first paragraph of 35 U.S.C. 112.

In addition, the application must be enabled at the time the invention was made.

6. The specification is objected to and claims 30-33 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention essentially for the reasons of record set forth in the previous Office Actions (Paper Nos. 21, 24, 27).

As indicated above in sections 5 and 6, there is insufficient information or guidance as "how to use" VCAM-1-specific antibodies in "a method of blocking interaction between a bone marrow stromal cells expressing VCAM-1 and a cell (hemopoietic precursor cell, hemopoietic stem or progenitor cells) expressing VLA-4 which comprises administering an antibody to VCAM-1 in an amount effective to decrease VCAM-1-mediated adhesion between the bone marrow stromal cell and a cell expressing VLA-4".

Applicant 's amendment, filed 9/19/97 (Paper No. 28), in conjunction with the submission of applicant's arguments and declaratory evidence, filed 8/22/97 (Paper No. 26) have been fully considered but are not found convincing for the reasons of record and reiterated above.

The application must be enabled at the time the invention was made.

As pointed out above in sections 5 and 6 and of record, the specification provides guidance and direction to applying the use of VCAM-1-specific antibodies to prevent GVHD (page 18, lines 11-12) as well as to prevent modulating the immune response or to impede lymphocyte or tumor cell transmigration (see Summary of the Invention, particularly page 4, lines 17-22). With respect to the use of hemopoietic cells, the specification provides guidance and direction to immunoselecting primitive hemopoietic stem cells, progenitor cells and bone marrow stromal elements (page 18, lines 13-15).

The examiner maintains that the application as filed does not provide written description nor guidance and direction on "how to use" anti-VCAM-1 to block any VCAM-1-mediated adhesion, regardless of the type of cells involved, to release bone marrow progenitor cells from the marrow to the peripheral blood or to mobilize hemopoietic cells.

Therefore, the specification as filed does not provide any guidance on "how to use" the VCAM-1 specific antibodies in the manner encompassed by the claims or argued by applicant in conjunction with Torok-Storb and Papayannoupoulo or any other manner as encompassed by the claimed methods. The specification is drawn to inhibiting lymphocyte adherence not hemopoietic stem and progenitor cell adherence. The disclosure does not provide direction or guidance as to which therapeutic conditions and what therapeutic endpoints are would be appropriate for the claimed methods.

Applicant's arguments are not found persuasive.

7. Upon reconsideration of the art and applicant 's amendments, filed 9/19/97 (Paper No. 28) and filed 8/22/97 (Paper No. 26); the previous rejection of claims 30 and 32-33 under 35 U.S.C. 112, first paragraph, for the scope of VCAM-1-specific antibodies has been withdrawn.

8. No claim allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[lila.feisee@uspto.gov]**.

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
September 30, 1997